

SEQUENCE LISTING

<110> The Regents of the University of California Baxter, John D Fletterick, Robert J Kushner, Peter J

<120> Nuclear Receptor Ligands and Ligand Binding Domains

<130> 407J-981114US

<140> US 10/827,121

<141> 2004-04-16

<160> 16

<170> PatentIn version 3.2

<210> 1

<211> 410

<212> PRT

<213> Rattus sp.

<400> 1

Met Glu Gln Lys Pro Ser Lys Val Glu Cys Gly Ser Asp Pro Glu Glu 1 5 10 15

Asn Ser Ala Arg Ser Pro Asp Gly. Lys Arg Lys Arg Lys Asn Gly Gln 20 25 30

Cys Pro Leu Lys Ser Ser Met Ser Gly Tyr Ile Pro Ser Tyr Leu Asp 35 40 45

Lys Asp Glu Gln Cys Val Val Cys Gly Asp Lys Ala Thr Gly Tyr His 50 60

Tyr Arg Cys Ile Thr Cys Glu Gly Cys Lys Gly Phe Phe Arg Arg Thr 65 70 75 80

Ile Gln Lys Asn Leu His Pro Thr Tyr Ser Cys Lys Tyr Asp Ser Cys 85 90 95

Cys Val Ile Asp Lys Ile Thr Arg Asn Gln Cys Gln Leu Cys Arg Phe 100 105 110

Lys Lys Cys Ile Ala Val Gly Met Ala Met Asp Leu Val Leu Asp Asp 115 120 125

Ser Lys Arg Val Ala Lys Arg Lys Leu Ile Glu Gln Asn Arg Glu Arg 130 135 140

Arg Arg Lys Glu Glu Met Ile Arg Ser Leu Gln Gln Arg Pro Glu Pro 145 150 155 160 Thr Pro Glu Glu Trp Asp Leu Ile His Val Ala Thr Glu Ala His Arg Ser Thr Asn Ala Gln Gly Ser His Trp Lys Gln Arg Arg Lys Phe Leu 180 185 190 Pro Asp Asp Ile Gly Gln Ser Pro Ile Val Ser Met Pro Asp Gly Asp 195 200 205 Lys Val Asp Leu Glu Ala Phe Ser Glu Phe Thr Lys Ile Ile Thr Pro 210 215 220 Ala Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Ser 235 230 235 Glu Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met 245 250 255 Glu Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Asp Thr Leu Thr Leu Ser Gly Glu Met Thr Val Lys Arg Lys Gln Leu Lys 275 280 285 Asn Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Glu Leu Gly Lys 290 295 300 Ser Leu Ser Ala Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln 305 310 315 Ala Val Leu Leu Met Ser Thr Asp Arg Ser Gly Leu Leu Cys Val Asp 325 Lys Ile Glu Lys Ser Gln Glu Ala Tyr Leu Leu Ala Phe Glu His Tyr 340 Val Asn His Arg Lys His Asn Ile Pro His Phe Trp Pro Lys Leu Leu 355 360 365 Met Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg 370 375 380 Phe Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu 390

Phe Leu Glu Val Phe Glu Asp Gln Glu Val 405 410 <211> 410

<212> PRT

<213> Homo sapiens

<400> 2

Met Glu Gln Lys Pro Ser Lys Val Glu Cys Gly Ser Asp Pro Glu Glu 1 5 10 15

Asn Ser Ala Arg Ser Pro Asp Gly Lys Arg Lys Asn Gly Gln 20 25 30

Cys Ser Leu Lys Thr Ser Met Ser Gly Tyr Ile Pro Ser Tyr Leu Asp 35 40 45

Lys Asp Glu Gln Cys Val Val Cys Gly Asp Lys Ala Thr Gly Tyr His 50 60

Tyr Arg Cys Ile Thr Cys Glu Gly Cys Lys Gly Phe Phe Arg Arg Thr 65 70 75 80

Ile Gln Lys Asn Leu His Pro Thr Tyr Ser Cys Lys Tyr Asp Ser Cys 85 90 95

Cys Val Ile Asp Lys Ile Thr Arg Asn Gln Cys Gln Leu Cys Arg Phe 100 105 110

Lys Lys Cys Ile Ala Val Gly Met Ala Met Asp Leu Val Leu Asp Asp 115 120 125

Ser Lys Arg Val Ala Lys Arg Lys Leu Ile Glu Gln Asn Arg Glu Arg 130 135 140

Arg Arg Lys Glu Glu Met Ile Arg Ser Leu Gln Gln Arg Pro Glu Pro 145 150 155 160

Thr Pro Glu Glu Trp Asp Leu Ile His Ile Ala Thr Glu Ala His Arg 165 170 175

Ser Thr Asn Ala Gln Gly Ser His Trp Lys Gln Arg Arg Lys Phe Leu 180 185 190

Pro Asp Asp Ile Gly Gln Ser Pro Ile Val Ser Met Pro Asp Gly Asp 195 200 205

Lys Val Asp Leu Glu Ala Phe Ser Glu Phe Thr Lys Ile Ile Thr Pro 210 215 220

Ala Ile Thr Arg Val Val Asp Phe Ala Lys Lys Leu Pro Met Phe Ser 235 230 235

Glu Leu Pro Cys Glu Asp Gln Ile Ile Leu Leu Lys Gly Cys Cys Met 245 250 255

Glu Ile Met Ser Leu Arg Ala Ala Val Arg Tyr Asp Pro Glu Ser Asp 260 265 270

Thr Leu Thr Leu Ser Gly Glu Met Ala Val Lys Arg Glu Gln Leu Lys 275 280 285

Asn Gly Gly Leu Gly Val Val Ser Asp Ala Ile Phe Glu Leu Gly Lys 290 295 300

Ser Leu Ser Ala Phe Asn Leu Asp Asp Thr Glu Val Ala Leu Leu Gln 305 310 315 320

Ala Val Leu Leu Met Ser Thr Asp Arg Ser Gly Leu Leu Cys Val Asp 325 330 335

Lys Ile Glu Lys Ser Gln Glu Ala Tyr Leu Leu Ala Phe Glu His Tyr 340 345 350

Val Asn His Arg Lys His Asn Ile Pro His Phe Trp Pro Lys Leu Leu 355 360 365

Met Lys Val Thr Asp Leu Arg Met Ile Gly Ala Cys His Ala Ser Arg 370 375 380

Phe Leu His Met Lys Val Glu Cys Pro Thr Glu Leu Phe Pro Pro Leu 385 390 395 400

Phe Leu Glu Val Phe Glu Asp Gln Glu Val 405

<210> 3

<211> 461

<212> PRT

<213> Homo sapiens

<400> 3

Met Thr Pro Asn Ser Met Thr Glu Asn Gly Leu Thr Ala Trp Asp Lys
1 10 15

Pro Lys His Cys Pro Asp Arg Glu His Asp Trp Lys Leu Val Gly Met 20 25 30

Ser Glu Ala Cys Leu His Arg Lys Ser His Ser Glu Arg Arg Ser Thr 35 40 45

Leu Lys Asn Glu Gln Ser Ser Pro His Leu Ile Gln Thr Thr Trp Thr

Ser Ser Ile Phe His Leu Asp His Asp Asp Val Asn Asp Gln Ser Val 65 70 75 80 Ser Ser Ala Gln Thr Phe Gln Thr Glu Glu Lys Lys Cys Lys Gly Tyr 85 90 95 Ile Pro Ser Tyr Leu Asp Lys Asp Glu Leu Cys Val Val Cys Gly Asp 100 105 110 Lys Ala Thr Gly Tyr His Tyr Arg Cys Ile Thr Cys Glu Gly Cys Lys 115 120 125 Gly Phe Phe Arg Arg Thr Ile Gln Lys Asn Leu His Pro Ser Tyr Ser 130 135 140 Cys Lys Tyr Glu Gly Lys Cys Val Ile Asp Lys Val Thr Arg Asn Gln 145 150 155 160 Cys Gln Glu Cys Arg Phe Lys Lys Cys Ile Tyr Val Gly Met Ala Thr 165 170 175 Asp Leu Val Leu Asp Asp Ser Lys Arg Leu Ala Lys Arg Lys Leu Ile 180 185 190 Glu Glu Asn Arg Glu Lys Arg Arg Glu Glu Leu Gln Lys Ser Ile 195 200 205 Gly His Lys Pro Glu Pro Thr Asp Glu Glu Trp Glu Leu Ile Lys Thr 210 215 220 Val Thr Glu Ala His Val Ala Thr Asn Ala Gln Gly Ser His Trp Lys 225 230 235 240 Gln Lys Pro Lys Phe Leu Pro Glu Asp Ile Gly Gln Ala Pro Ile Val 245 250 255 Asn Ala Pro Glu Gly Gly Lys Val Asp Leu Glu Ala Phe Ser His Phe 260 265 270 Thr Lys Ile Ile Thr Pro Ala Ile Thr Arg Val Val Asp Phe Ala Lys 275 280 285 Lys Leu Pro Met Phe Cys Glu Leu Pro Cys Glu Asp Gln Ile Ile Leu 290 295 300 Leu Lys Gly Cys Cys Met Glu Ile Met Ser Leu Arg Ala Ala Val Arg 305 310 315 320 Tyr Asp Pro Glu Ser Glu Thr Leu Thr Leu Asn Gly Glu Met Ala Val 325 330 335

Ile Arg Gly Gln Leu Lys Asn Gly Gly Leu Gly Val Val Ser Asp Ala 340 345 350

Ile Phe Asp Leu Gly Met Ser Leu Ser Ser Phe Asn Leu Asp Asp Thr 355 360 365

Glu Val Ala Leu Leu Gln Ala Val Leu Leu Met Ser Ser Asp Arg Pro 370 380

Gly Leu Ala Cys Val Glu Arg Ile Glu Lys Tyr Gln Asp Ser Phe Leu 385 390 395 400

Leu Ala Phe Glu His Tyr Ile Asn Tyr Arg Lys His His Val Thr His
405 410 415

Phe Trp Pro Lys Leu Leu Met Lys Val Thr Asp Leu Arg Met Ile Gly 420 425 430

Ala Cys His Ala Ser Arg Phe Leu His Met Lys Val Glu Cys Pro Thr

Glu Leu Leu Pro Pro Leu Phe Leu Glu Val Phe Glu Asp

<210> <211> 416

<212> **PRT** Homo sapiens

<400>

Pro Asn Ser Asn His Val Ala Ser Gly Ala Gly Glu Ala Ala Ile Glu
1 5 10 15

Thr Gln Ser Ser Ser Glu Glu Ile Val Pro Ser Pro Pro Ser Pro 20 25 30

Pro Pro Leu Pro Arg Ile Tyr Lys Pro Cys Phe Val Cys Gln Asp Lys 35 40 45

Ser Ser Gly Tyr His Tyr Gly Val Ser Ala Cys Glu Gly Cys Lys Gly
50 60

Phe Phe Arg Arg Ser Ile Gln Lys Asn Met Val Tyr Thr Cys His Arg 65 70 75 80

Asp Lys Asn Cys Ile Ile Asn Lys Val Thr Arg Asn Arg Cys Gln Tyr Cys Arg Leu Gln Lys Cys Phe Glu Val Gly Met Ser Lys Glu Ser Val Arg Asn Asp Arg Asn Lys Lys Lys Glu Val Pro Lys Pro Glu Cys 115 120 125 Ser Glu Ser Tyr Thr Leu Thr Pro Glu Val Gly Glu Leu Ile Glu Lys Val Arg Lys Ala His Gln Glu Thr Phe Pro Ala Leu Cys Gln Leu Gly 145 150 155 160 Lys Tyr Thr Thr Asn Asn Ser Ser Glu Gln Arg Val Ser Leu Asp Ile Asp Leu Trp Asp Lys Phe Ser Glu Leu Ser Thr Lys Cys Ile Ile Lys 180 185 190 Thr Val Glu Phe Ala Lys Gln Leu Pro Gly Phe Thr Thr Leu Thr Ile Ala Asp Gln Ile Thr Leu Leu Lys Ala Ala Cys Leu Asp Ile Leu Ile 210 215 220 Leu Arg Ile Cys Thr Arg Tyr Thr Pro Glu Gln Asp Thr Met Thr Phe 225 230 235 240 Ser Asp Gly Leu Thr Leu Asn Arg Thr Gln Met His Asn Ala Gly Phe 245 250 255 Gly Pro Leu Thr Asp Leu Val Phe Ala Phe Ala Asn Gln Leu Leu Pro Leu Glu Met Asp Asp Ala Glu Thr Gly Ile Leu Ser Ala Ile Cys Leu Ile Cys Gly Asp Arg Gln Asp Leu Glu Gln Pro Asp Arg Val Asp Met 290 295 300 Leu Gln Glu Pro Leu Leu Glu Ala Leu Lys Val Tyr Val Arg Lys Arg 305 Arg Pro Ser Arg Pro His Met Phe Pro Lys Met Leu Met Lys Ile Thr 325 330 335 Asp Leu Arg Ser Ile Ser Ala Lys Gly Ala Glu Arg Val Ile Thr Leu

345 . 350 340

Lys Met Glu Ile Pro Gly Ser Met Pro Pro Leu Ile Gln Glu Met Leu 355 360 365

Glu Asn Ser Glu Gly Leu Asp Thr Leu Ser Gly Gln Pro Gly Gly 370 380

Gly Arg Asp Gly Gly Leu Ala Pro Pro Pro Gly Ser Cys Ser Pro 385 390 395 400

Ser Leu Ser Pro Ser Ser Asn Arg Ser Ser Pro Ala Thr His Ser Pro 405 410 415

<210> <211> <212> 454

PRT Homo sapiens

<400>

Met Ala Thr Asn Lys Glu Arg Leu Phe Ala Ala Gly Ala Leu Gly Pro 1 10 15

Gly Ser Gly Tyr Pro Gly Ala Gly Phe Pro Phe Ala Phe Pro Gly Ala 20 25 30

Leu Arg Gly Ser Pro Pro Phe Glu Met Leu Ser Pro Ser Phe Arg Gly 35 40 45

Leu Gly Gln Pro Asp Leu Pro Lys Glu Met Ala Ser Leu Ser Val Glu 50 55 60

Thr Gln Ser Thr Ser Ser Glu Glu Met Val Pro Ser Ser Pro 65 70 75 80

Pro Pro Pro Arg Val Tyr Lys Pro Cys Phe Val Cys Asn Asp Lys 85 90 95

Ser Ser Gly Tyr His Tyr Gly Val Ser Ser Cys Glu Gly Cys Lys Gly 100 105 110

Phe Phe Arg Arg Ser Ile Gln Lys Asn Met Val Tyr Thr Cys His Arg 115 120 125

Asp Lys Asn Cys Ile Ile Asn Lys Val Thr Arg Asn Arg Cys Gln Tyr 130 135 140

Cys Arg Leu Gln Lys Cys Phe Glu Val Gly Met Ser Lys Glu Ala Val 145 150 155 160

Arg Asn Asp Arg Asn Lys Lys Lys Glu Val Lys Glu Glu Gly Ser 165 170 175 Pro Asp Ser Tyr Glu Leu Ser Pro Gln Leu Glu Glu Leu Ile Thr Lys 180 185 190 Val Ser Lys Ala His Gln Glu Thr Phe Pro Ser Leu Cys Gln Leu Gly 195 200 205 Lys Tyr Thr Thr Asn Ser Ser Ala Asp His Arg Val Gln Leu Asp Leu 210 220 Gly Leu Trp Asp Lys Phe Ser Glu Leu Ala Thr Lys Cys Ile Ile Lys 235 230 235 Ile Val Glu Phe Ala Lys Arg Leu Pro Gly Phe Thr Gly Leu Ser Ile 245 250 255 Ala Asp Gln Ile Thr Leu Leu Lys Ala Ala Cys Leu Asp Ile Leu Met 260 265 270 Leu Arg Ile Cys Thr Arg Tyr Thr Pro Glu Gln Asp Thr Met Thr Phe 275 280 285 Ser Asp Gly Leu Thr Leu Asn Arg Thr Gln Met His Asn Ala Gly Phe 290 295 300 Gly Pro Leu Thr Asp Leu Val Phe Ala Phe Ala Gly Gln Leu Leu Pro 305 310 315 320 Leu Glu Met Asp Asp Thr Glu Thr Gly Leu Leu Ser Ala Ile Cys Leu 325 330 335 . Ile Cys Gly Asp Arg Met Asp Leu Glu Glu Pro Glu Lys Val Asp Lys 345 350 Leu Gln Glu Pro Leu Leu Glu Ala Leu Arg Leu Tyr Ala Arg Arg Arg Pro Ser Gln Pro Tyr Met Phe Pro Arg Met Leu Met Lys Ile Thr 370 380 Asp Leu Arg Gly Ile Ser Thr Lys Gly Ala Glu Arg Ala Ile Thr Leu 385 390 395 400 Lys Met Glu Ile Pro Gly Pro Met Pro Pro Leu Ile Arg Glu Met Leu

Glu Asn Pro Glu Met Phe Glu Asp Asp Ser Ser Gln Pro Gly Pro His 420 425 430

Pro Asn Ala Ser Ser Glu Asp Glu Val Pro Gly Gly Gln Gly Lys Gly
435 440 445

Gly Leu Lys Ser Pro Ala 450

<210> 6

<211> 462

<212> PRT

<213> Homo sapiens

<400> 6

Met Asp Thr Lys His Phe Leu Pro Leu Asp Phe Ser Thr Gln Val Asn 1 5 10 15

Ser Ser Leu Thr Ser Pro Thr Gly Arg Gly Ser Met Ala Ala Pro Ser 20 25 30

Leu His Pro Ser Leu Gly Pro Gly Ile Gly Ser Pro Gly Gln Leu His 35 40 45

Ser Pro Ile Ser Thr Leu Ser Ser Pro Ile Asn Gly Met Gly Pro Pro 50 60

Phe Ser Val Ile Ser Ser Pro Met Gly Pro His Ser Met Ser Val Pro 65 70 75 80

Thr Thr Pro Thr Leu Gly Phe Ser Thr Gly Ser Pro Gln Leu Ser Ser 85 90 95

Pro Met Asn Pro Val Ser Ser Glu Asp Ile Lys Pro Pro Leu Gly
100 105 110

Leu Asn Gly Val Leu Lys Val Pro Ala His Pro Ser Gly Asn Met Ala 115 120 125

Ser Phe Thr Lys His Ile Cys Ala Ile Cys Gly Asp Arg Ser Ser Gly 130 135 140

Lys His Tyr Gly Val Tyr Ser Cys Glu Gly Cys Lys Gly Phe Phe Lys 145 150 155 160

Arg Thr Val Arg Lys Asp Leu Thr Tyr Thr Cys Arg Asp Asn Lys Asp 165 170 175

Cys Leu Ile Asp Lys Arg Gln Arg Asn Arg Cys Gln Tyr Cys Arg Tyr 180 185 190 Gln Lys Cys Leu Ala Met Gly Met Lys Arg Glu Ala Val Gln Glu Glu 195 200 205 Gln Arg Gly Lys Asp Arg Asn Glu Asn Glu Val Glu Ser Thr Ser 210 220 Ser Ala Asn Glu Asp Met Pro Val Glu Arg Ile Leu Glu Ala Glu Leu 225 230 235 240 Ala Val Glu Pro Lys Thr Glu Thr Tyr Val Glu Ala Asn Met Gly Leu 245 250 255 Asn Pro Ser Ser Pro Asn Asp Pro Val Thr Asn Ile Cys Gln Ala Ala Lys Gln Leu Phe Thr Leu Val Glu Trp Ala Lys Arg Ile Pro His 275 280 285 Ser Glu Leu Pro Leu Asp Asp Gln Val Ile Leu Leu Arg Ala Gly 290 295 300 Trp Asn Glu Leu Leu Ile Ala Ser Phe Ser His Arg Ser Ile Ala Val 305 310 315 320 Lys Asp Gly Ile Leu Leu Ala Thr Gly Leu His Val His Arg Asn Ser Ala His Ser Ala Gly Val Gly Ala Ile Phe Asp Arg Val Leu Thr Glu 350 Leu Val Ser Lys Met Arg Asp Met Gln Met Asp Lys Thr Glu Leu Gly 355 360 365 Cys Leu Arg Ala Ile Val Leu Phe Asn Pro Asp Ser Lys Gly Leu Ser 370 380 Asn Pro Ala Glu Val Glu Ala Leu Arg Glu Lys Val Tyr Ala Ser Leu 385 390 395 400 Glu Ala Tyr Cys Lys His Lys Tyr Pro Glu Gln Pro Gly Arg Phe Ala 405 410 415 Lys Leu Leu Arg Leu Pro Ala Leu Arg Ser Ile Gly Leu Lys Cys 420 425 430 Glu His Leu Phe Phe Phe Lys Leu Ile Gly Asp Thr Pro Ile Asp 445 Thr Phe Leu Met Glu Met Leu Glu Ala Pro His Gln Met Thr 450 455 460

<210> 7

<211> 525

<212> PRT

<213> Homo sapiens

<400> 7

Met Ser Trp Ala Ala Arg Pro Pro Phe Leu Pro Gln Arg His Ala Glu 1 5 10 15

Gly Ser Val Gly Arg Trp Gly Ala Lys Glu Cys Ile Val Gly Ser Ala 20 25 30

Thr Ala Leu Ala Gly Ser Arg Ser Gly Gly Gly Gly Gly Gly Arg
35 40 45

Asp Gly Arg His Gly Arg Asp Ser Arg Ser Pro Asp Ser Ser Ser Pro 65 70 75 80

Asn Pro Leu Pro Gln Gly Val Pro Pro Pro Ser Pro Pro Gly Pro Pro 85 90 95

Leu Pro Pro Ser Thr Ala Pro Thr Leu Gly Gly Ser Gly Ala Pro Pro 100 105 110

Pro Pro Pro Met Pro Pro Pro Leu Gly Ser Pro Phe Pro Val Ile 115 120 125

Ser Ser Ser Met Gly Ser Pro Gly Leu Pro Pro Pro Ala Pro Pro Gly 130 140

Phe Ser Gly Pro Val Ser Ser Pro Gln Ile Asn Ser Thr Val Ser Leu 145 150 155 160

Pro Gly Gly Ser Gly Pro Pro Glu Asp Val Lys Pro Pro Val Leu 165 170 175

Gly Val Arg Gly Leu His Cys Pro Pro Pro Pro Gly Gly Pro Gly Ala 180 185 190

Gly Lys Arg Leu Cys Ala Ile Cys Gly Asp Arg Ser Ser Gly Lys His 195 200 205

Tyr Gly Val Tyr Ser Cys Glu Gly Cys Lys Gly Phe Phe Lys Arg Thr

Ile Arg Lys Asp Leu Thr Tyr Ser Cys Arg Asp Asn Lys Asp Cys Thr 225 230 235 240 Val Asp Lys Arg Gln Arg Asn Arg Cys Gln Tyr Cys Arg Tyr Gln Lys 245 250 255 Cys Leu Ala Thr Gly Met Lys Arg Glu Ala Val Gln Glu Glu Arg Ġln 260 265 270 Arg Gly Lys Asp Lys Asp Gly Asp Gly Glu Cys Ala Gly Gly Ala Pro 275 280 285 Glu Glu Met Pro Val Asp Arg Ile Leu Glu Ala Glu Leu Ala Val Glu 290 295 300 Gln Lys Ser Asp Gln Gly Val Glu Gly Pro Gly Gly Thr Gly Gly Ser 305 310 315 Gly Ser Ser Pro Asn Asp Pro Val Thr Asn Ile Cys Gln Ala Ala Asp 325 330 335 Lys Gln Leu Phe Thr Leu Val Glu Trp Ala Lys Arg Ile Pro His Phe 340 345 350 Ser Ser Leu Pro Leu Asp Asp Gln Val Ile Leu Leu Arg Ala Gly Trp 355 360 365 Asn Glu Leu Leu Ile Ala Ser Phe Ser His Arg Ser Ile Asp Val Arg 370 375 380 Asp Gly Ile Leu Leu Ala Thr Gly Leu His Val His Arg Asn Ser Ala 385 390 395 400 His Ser Ala Gly Val Gly Ala Ile Phe Asp Arg Val Leu Thr Glu Leu 405 410 415 Val Ser Lys Met Arg Asp Met Arg Met Asp Lys Thr Glu Leu Gly Cys 420 425 430 Leu Arg Ala Ile Ile Leu Phe Asn Pro Asp Ala Lys Gly Leu Ser Asn 435 440 445 Pro Ser Glu Val Glu Val Leu Arg Glu Lys Val Tyr Ala Ser Leu Glu 450 460 Thr Tyr Cys Lys Gln Lys Tyr Pro Glu Gln Gln Gly Arg Phe Ala Lys 465 470 475 480 Leu Leu Leu Arg Leu Pro Ala Leu Arg Ser Ile Gly Leu Lys Cys Leu 485 490 495

Glu His Leu Phe Phe Phe Lys Leu Ile Gly Asp Thr Pro Ile Asp Thr 500 505 510

Phe Leu Met Glu Met Leu Glu Ala Pro His Gln Leu Ala 515 520 525

<210> 8

<211> 468 <212> PRT

<213> Homo sapiens

<400> 8

Met Val Asp Thr Glu Ser Pro Leu Cys Pro Leu Ser Pro Leu Glu Ala 1 5 10 15

Gly Asp Leu Glu Ser Pro Leu Ser Glu Glu Phe Leu Gln Glu Met Gly 20 25 30

Asn Ile Gln Glu Ile Ser Gln Ser Ile Gly Glu Asp Ser Ser Gly Ser 35 40 45

Phe Gly Phe Thr Glu Tyr Gln Tyr Leu Gly Ser Cys Pro Gly Ser Asp 50 55 60

Gly Ser Val Ile Thr Asp Thr Leu Ser Pro Ala Ser Ser Pro Ser Ser 65 70 75 80

Val Thr Tyr Pro Val Val Pro Gly Ser Val Asp Glu Ser Pro Ser Gly 85 90 95

Ala Leu Asn Ile Glu Cys Arg Ile Cys Gly Asp Lys Ala Ser Gly Tyr 100 105 110

His Tyr Gly Val His Ala Cys Glu Gly Cys Lys Gly Phe Phe Arg Arg 115 120 125

Thr Ile Arg Leu Lys Leu Val Tyr Asp Lys Cys Asp Arg Ser Cys Lys 130 135 140

Ile Gln Lys Lys Asn Arg Asn Lys Cys Gln Tyr Cys Arg Phe His Lys 145 150 155 160

Cys Leu Ser Val Gly Met Ser His Asn Ala Ile Arg Phe Gly Arg Met 165 170 175 Pro Arg Ser Glu Lys Ala Lys Leu Lys Ala Glu Ile Leu Thr Cys Glu 180 185 190 His Asp Ile Glu Asp Ser Glu Thr Ala Asp Leu Lys Ser Leu Ala Lys Arg Ile Tyr Glu Ala Tyr Leu Lys Asn Phe Asn Met Asn Lys Val Lys 210 220 Ala Arg Val Ile Leu Ser Gly Lys Ala Ser Asn Asn Pro Pro Phe Val Ile His Asp Met Glu Thr Leu Cys Met Ala Glu Lys Thr Leu Val Ala Lys Leu Val Ala Asn Gly Ile Gln Asn Lys Glu Val Glu Val Arg Ile Phe His Cys Cys Gln Cys Thr Ser Val Glu Thr Val Thr Glu Leu Thr 275 280 285 Glu Phe Ala Lys Ala Ile Pro Ala Phe Ala Asn Leu Asp Leu Asn Asp Gln Val Thr Leu Leu Lys Tyr Gly Val Tyr Glu Ala Ile Phe Ala Met Leu Ser Ser Val Met Asn Lys Asp Gly Met Leu Val Ala Tyr Gly Asn 325 330 335 Gly Phe Ile Thr Arg Glu Phe Leu Lys Ser Leu Arg Lys Pro Phe Cys 340 Asp Ile Met Glu Pro Lys Phe Asp Phe Ala Met Lys Phe Asn Ala Leu 355 Glu Leu Asp Asp Ser Asp Ile Ser Leu Phe Val Ala Ala Ile Ile Cys 370 Cys Gly Asp Arg Pro Gly Leu Leu Asn Val Gly His Ile Glu Lys Met 385 390 395 400 Gln Glu Gly Ile Val His Val Leu Arg Leu His Leu Gln Ser Asn His 410 Asp Asp Ile Phe Leu Phe Pro Lys Leu Leu Gln Lys Met Ala Asp 420 425 430 420 Leu Arg Gln Leu Val Thr Glu His Ala Gln Leu Val Gln Ile Ile Lys 435

Lys Thr Glu Ser Asp Ala Ala Leu His Pro Leu Leu Gln Glu Ile Tyr 450 455 460

Arg Asp Met Tyr 465

<210> 9

<211> 441 <212> PRT

<213> Homo sapiens

<400> 9

Met Glu Gln Pro Gln Glu Glu Ala Pro Glu Val Arg Glu Glu Glu 1 5 10 15

Lys Glu Glu Val Ala Glu Ala Glu Gly Ala Pro Glu Leu Asn Gly Gly 20 25 30

Pro Gln His Ala Leu Pro Ser Ser Ser Tyr Thr Asp Leu Ser Arg Ser 35 40 45

Ser Ser Pro Pro Ser Leu Leu Asp Gln Leu Gln Met Gly Cys Asp Gly
50 60

Ala Ser Cys Gly Ser Leu Asn Met Glu Cys Arg Val Cys Gly Asp Lys 65 70 75 80

Ala Ser Gly Phe His Tyr Gly Val His Ala Cys Glu Gly Cys Lys Gly 85 90 95

Phe Phe Arg Arg Thr Ile Arg Met Lys Leu Glu Tyr Glu Lys Cys Glu . 100 105 110

Arg Ser Cys Lys Ile Gln Lys Lys Asn Arg Asn Lys Cys Gln Tyr Cys 115 120 125

Arg Phe Gln Lys Cys Leu Ala Leu Gly Met Ser His Asn Ala Ile Arg 130 135 140

Phe Gly Arg Met Pro Glu Ala Glu Lys Arg Lys Leu Val Ala Gly Leu 145 150 155 160

Thr Ala Asn Glu Gly Ser Gln Tyr Asn Pro Gln Val Ala Asp Leu Lys 165 170 175

Ala Phe Ser Lys His Ile Tyr Asn Ala Tyr Leu Lys Asn Phe Asn Met 180 185 190 Thr Lys Lys Ala Arg Ser Ile Leu Thr Gly Lys Ala Ser His Thr 195 200 205 Ala Pro Phe Val Ile His Asp Ile Glu Thr Leu Trp Gln Ala Glu Lys 210 220 Gly Leu Val Trp Lys Gln Leu Val Asn Gly Leu Pro Pro Tyr Lys Glu 225 230 235 240 Ile Ser Val His Val Phe Tyr Arg Cys Gln Cys Thr Thr Val Glu Thr Val Arg Glu Leu Thr Glu Phe Ala Lys Ser Ile Pro Ser Phe Ser Ser 260 265 270 260 Leu Phe Leu Asn Asp Gln Val Thr Leu Leu Lys Tyr Gly Val His Glu 275 280 285 Ala Ile Phe Ala Met Leu Ala Ser Ile Val Asn Lys Asp Gly Leu Leu 290 295 300 Val Ala Asn Gly Ser Gly Phe Val Thr Arg Glu Phe Leu Arg Ser Leu 305 310 315 320 Arg Lys Pro Phe Ser Asp Ile Ile Glu Pro Lys Phe Glu Phe Ala Val 325 330 335 Lys Phe Asn Ala Leu Glu Leu Asp Asp Ser Asp Leu Ala Leu Phe Ile 340 345 350 Ala Ala Ile Ile Leu Cys Gly Asp Arg Pro Gly Leu Met Asn Val Pro 355 360 365 Val Glu Ala Ile Gln Asp Thr Ile Leu Arg Ala Leu Glu Phe His 370 380 Leu Gln Ala Asn His Pro Asp Ala Gln Tyr Leu Phe Pro Lys Leu Leu 385 390 Gln Lys Met Ala Asp Leu Arg Gln Leu Val Thr Glu His Ala Gln Met Met Gln Arg Ile Lys Lys Thr Glu Thr Glu Thr Ser Leu His Pro Leu Leu Gln Glu Ile Tyr Lys Asp Met Tyr

<210> 10

<211> 475

<212> PRT

<213> Homo sapiens

<400> 10

Met Val Asp Thr Glu Met Pro Phe Trp Pro Thr Asn Phe Gly Ile Ser $10 \hspace{1cm} 15$

Ser Val Asp Leu Ser Met Met Asp Asp His Ser His Ser Phe Asp Ile 20 25 30

Lys Pro Phe Thr Thr Val Asp Phe Ser Ser Ile Ser Ala Pro His Tyr 35 40 45

Glu Asp Ile Pro Phe Thr Arg Ala Asp Pro Met Val Ala Asp Tyr Lys 50 60

Tyr Asp Leu Lys Leu Gln Glu Tyr Gln Ser Ala Ile Lys Val Glu Pro 65 70 75 80

Ala Ser Pro Pro Tyr Tyr Ser Glu Lys Ala Gln Leu Tyr Asn Arg Pro 85 90 95

His Glu Glu Pro Ser Asn Ser Leu Met Ala Ile Glu Cys Arg Val Cys 100 105 110

Gly Asp Lys Ala Ser Gly Phe His Tyr Gly Val His Ala Cys Glu Gly 115 120 125

Cys Lys Gly Phe Phe Arg Arg Thr Ile Arg Leu Lys Leu Ile Tyr Asp 130 140

Arg Cys Asp Leu Asn Cys Arg Ile His Lys Lys Ser Arg Asn Lys Cys 145 150 155 160

Gln Tyr Cys Arg Phe Gln Lys Cys Leu Ala Val Gly Met Ser His Asn 165 170 175

Ala Ile Arg Phe Gly Arg Met Pro Gln Ala Glu Lys Glu Lys Leu Leu 180 . 185 . 190

Ala Glu Ile Ser Ser Asp Ile Asp Gln Leu Asn Pro Glu Ser Ala Asp 195 200 205

Leu Arg Ala Leu Ala Lys His Leu Tyr Asp Ser Tyr Ile Lys Ser Phe 210 215 220

Pro Leu Thr Lys Ala Lys Ala Arg Ala Ile Leu Thr Gly Lys Thr Thr 225 230 235 240

Asp Lys Ser Pro Phe Val Ile Tyr Asp Met Asn Ser Leu Met Met Gly 250 Glu Asp Lys Ile Lys Phe Lys His Ile Thr Pro Leu Gln Glu Gln Ser 260 265 . 270 Lys Glu Val Ala Ile Arg Ile Phe Gln Gly Cys Gln Phe Arg Ser Val Glu Ala Val Gln Glu Ile Thr Glu Tyr Ala Lys Asn Ile Pro Gly Phe 295 300 Ile Asn Leu Asp Leu Asn Asp Gln Val Thr Leu Leu Lys Tyr Gly Val 305 310 His Glu Ile Ile Tyr Thr Met Leu Ala Ser Leu Met Asn Lys Asp Gly 325 330 335 Val Leu Ile Ser Glu Gly Gln Gly Phe Met Thr Arg Glu Phe Leu Lys Ser Leu Arg Lys Pro Phe Gly Asp Phe Met Glu Pro Lys Phe Glu Phe 355 360 . 365 Ala Val Lys Phe Asn Ala Leu Glu Leu Asp Asp Ser Asp Leu Ala Ile Phe Ile Ala Val Ile Ile Leu Ser Gly Asp Arg Pro Gly Leu Leu Asn 385 395 400 385 390 Val Lys Pro Ile Glu Asp Ile Gln Asp Asn Leu Leu Gln Ala Leu Glu 405 Leu Gln Leu Lys Leu Asn His Pro Glu Ser Ser Gln Leu Phe Ala Lys 420 425 430 Val Leu Gln Lys Met Thr Asp Leu Arg Gln Ile Val Thr Glu His Val Gln Leu Leu His Val Ile Lys Lys Thr Glu Thr Asp Met Ser Leu His 450 455 460 Pro Leu Leu Gln Glu Ile Tyr Lys Asp Leu Tyr 470 475

470

<210> 11 427 <211> PRT

<213> Homo sapiens

<400> 11

Met Glu Ala Met Ala Ala Ser Thr Ser Leu Pro Asp Pro Gly Asp Phe 1 5 10 15

Asp Arg Asn Val Pro Arg Ile Cys Gly Val Cys Gly Asp Arg Ala Thr 20 25 30

Gly Phe His Phe Asn Ala Met Thr Cys Glu Gly Cys Lys Gly Phe Phe 35 40 45

Arg Arg Ser Met Lys Arg Lys Ala Leu Phe Thr Cys Pro Phe Asn Gly 50 60

Asp Cys Arg Ile Thr Lys Asp Asn Arg Arg His Cys Gln Ala Cys Arg 65 70 75 80

Leu Lys Arg Cys Val Asp Ile Gly Met Met Lys Glu Phe Ile Leu Thr 85 90 95

Asp Glu Glu Val Gln Arg Lys Arg Glu Met Ile Leu Lys Arg Lys Glu
100 105 110

Glu Glu Ala Leu Lys Asp Ser Leu Arg Pro Lys Leu Ser Glu Glu Gln 115 120 125

Gln Arg Ile Ile Ala Ile Leu Leu Asp Ala His His Lys Thr Tyr Asp 130 135 140

Pro Thr Tyr Ser Asp Phe Cys Gln Phe Arg Pro Pro Val Arg Val Asn 145 150 155 160

Asp Gly Gly Ser His Pro Ser Arg Pro Asn Ser Arg His Thr Pro 165 170 175

Ser Phe Ser Gly Asp Ser Ser Ser Ser Cys Ser Asp His Cys Ile Thr 180 185 190

Ser Ser Asp Met Met Asp Ser Ser Ser Phe Ser Asn Leu Asp Leu Ser 195 200 205

Glu Glu Asp Ser Asp Asp Pro Ser Val Thr Leu Glu Leu Ser Gln Leu 210 215 220

Ser Met Leu Pro His Leu Ala Asp Leu Val Ser Tyr Ser Ile Gln Lys 225 230 235 240

Val Ile Gly Phe Ala Lys Met Ile Pro Gly Phe Arg Asp Leu Thr Ser

Glu Asp Gln Ile Val Leu Leu Lys Ser Ser Ala Ile Glu Val Ile Met 260 265 270

Leu Arg Ser Asn Glu Ser Phe Thr Met Asp Asp Met Ser Trp Thr Cys 275 280 285

Gly Asn Gln Asp Tyr Lys Tyr Arg Val Ser Asp Val Thr Lys Ala Gly 290 295 300

His Ser Leu Glü Leu Ile Glu Pro Leu Ile Lys Phe Gln Val Gly Leu 305 310 315 320

Lys Lys Leu Asn Leu His Glu Glu Glu His Val Leu Leu Met Ala Ile 325 330 335

Cys Ile Val Ser Pro Asp Arg Pro Gly Val Gln Asp Ala Ala Leu Ile 340 345 350

Glu Ala Ile Gln Asp Arg Leu Ser Asn Thr Leu Gln Thr Tyr Ile Arg 355 360 365

Cys Arg His Pro Pro Pro Gly Ser His Leu Leu Tyr Ala Lys Met Ile 370 375 380

Gln Lys Leu Ala Asp Leu Arg Ser Leu Asn Glu Glu His Ser Lys Gln 385 390 395 400

Tyr Arg Cys Leu Ser Phe Gln Pro Glu Cys Ser Met Lys Leu Thr Pro 405 410 415

Leu Val Leu Glu Val Phe Gly Asn Glu Ile Ser 420 425

<210> 12

<211> 595

<212> PRT

<213> Homo sapiens

<400> 12

Met Thr Met Thr Leu His Thr Lys Ala Ser Gly Met Ala Leu Leu His 1 10 15

Gln Ile Gln Gly Asn Glu Leu Glu Pro Leu Asn Arg Pro Gln Leu Lys 20 25 30

Ile Pro Leu Glu Arg Pro Leu Gly Glu Val Tyr Leu Asp Ser Ser Lys 35 40 45

Pro Ala Val Tyr Asn Tyr Pro Glu Gly Ala Ala Tyr Glu Phe Asn Ala 50 55 60 Ala Ala Ala Asn Ala Gln Val Tyr Gly Gln Thr Gly Leu Pro Tyr 65 70 75 80 Gly Pro Gly Ser Glu Ala Ala Ala Phe Gly Ser Asn Gly Leu Gly Gly 85 90 95 Phe Pro Pro Leu Asn Ser Val Ser Pro Ser Pro Leu Met Leu Leu His Pro Pro Pro Gln Leu Ser Pro Phe Leu Gln Pro His Gly Gln Gln Val 115 120 125 Pro Tyr Tyr Leu Glu Asn Glu Pro Ser Gly Tyr Thr Val Arg Glu Ala 130 135 140 Gly Pro Pro Ala Phe Tyr Arg Pro Asn Ser Asp Asn Arg Arg Gln Gly
145 150 155 . 160 Gly Arg Glu Arg Leu Ala Ser Thr Asn Asp Lys Gly Ser Met Ala Met 165 170 175 Glu Ser Ala Lys Glu Thr Arg Tyr Cys Ala Val Cys Asn Asp Tyr Ala 180 185 190 Ser Gly Tyr His Tyr Gly Val Trp Ser Cys Glu Gly Cys Lys Ala Phe 195 200 205 Phe Lys Arg Ser Ile Gln Gly His Asn Asp Tyr Met Cys Pro Ala Thr 210 215 220 Asn Gln Cys Thr Ile Asp Lys Asn Arg Arg Lys Ser Cys Gln Ala Cys 235 230 240 Arg Leu Arg Lys Cys Tyr Glu Val Gly Met Met Lys Gly Gly Ile Arg 245 250 255 Lys Asp Arg Arg Gly Gly Arg Met Leu Lys His Lys Arg Gln Arg Asp 260 265 270 Asp Gly Glu Gly Arg Gly Glu Val Gly Ser Ala Gly Asp Met Arg Ala 275 280 285 Ala Asn Leu Trp Pro Ser Pro Leu Met Ile Lys Arg Ser Lys Lys Asn 290 295 300

Ser Leu Ala Leu Ser Leu Thr Ala Asp Gln Met Val Ser Ala Leu Leu 305 Asp Ala Glu Pro Pro Ile Leu Tyr Ser Glu Tyr Asp Pro Thr Arg Pro 325 330 335 Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn Leu Ala Asp Arg Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val Pro Gly Phe Val Asp Leu Thr Leu His Asp Gln Val His Leu Leu Glu Cys Ala Trp Leu Glu Ile Leu Met Ile Gly Leu Val Trp Arg Ser Met Glu His Pro Gly 385 390 395 400 Lys Leu Leu Phe Ala Pro Asn Leu Leu Leu Asp Arg Asn Gln Gly Lys
405
410
415 Cys Val Glu Gly Met Val Glu Ile Phe Asp Met Leu Leu Ala Thr Ser Ser Arg Phe Arg Met Met Asn Leu Gln Gly Glu Glu Phe Val Cys Leu Lys Ser Ile Ile Leu Leu Asn Ser Gly Val Tyr Thr Phe Leu Ser Ser 450 Thr Leu Lys Ser Leu Glu Glu Lys Asp His Ile His Arg Val Leu Asp 465 Lys Ile Thr Asp Thr Leu Ile His Leu Met Ala Lys Ala Gly Leu Thr Leu Gln Gln His Gln Arg Leu Ala Gln Leu Leu Leu Ile Leu Ser 500 His Ile Arg His Met Ser Asn Lys Gly Met Glu His Leu Tyr Ser Met 515 520 525 Lys Cys Lys Asn Val Val Pro Leu Tyr Asp Leu Leu Glu Met Leu 530 540 Asp Ala His Arg Leu His Ala Pro Thr Ser Arg Gly Gly Ala Ser Val 545 550 555 560 Glu Glu Thr Asp Gln Ser His Leu Ala Thr Ala Gly Ser Thr Ser Ser

565 570 575

His Ser Leu Gln Lys Tyr Tyr Ile Thr Gly Glu Ala Glu Gly Phe Pro 580 585 590

Ala Thr Val 595

<210> 13

<211> 777 <212> PRT

<213> Homo sapiens

<400> 13

Met Asp Ser Lys Glu Ser Leu Thr Pro Gly Arg Glu Glu Asn Pro Ser 1 10 15

Ser Val Leu Ala Gln Glu Arg Gly Asp Val Met Asp Phe Tyr Lys Thr 20 25 30

Leu Arg Gly Gly Ala Thr Val Lys Val Ser Ala Ser Ser Pro Ser Leu 35 40 45

Ala Val Ala Ser Gln Ser Asp Ser Lys Gln Arg Arg Leu Leu Val Asp 50 55 60

Phe Pro Lys Gly Ser Val Ser Asn Ala Gln Gln Pro Asp Leu Ser Lys 65 70 75 80

Ala Val Ser Leu Ser Met Gly Leu Tyr Met Gly Glu Thr Glu Thr Lys 85 90 95

Val Met Gly Asn Asp Leu Gly Phe Pro Gln Gln Gly Gln Ile Ser Leu $100 \hspace{1cm} 105 \hspace{1cm} 110$

Ser Ser Gly Glu Thr Asp Leu Lys Leu Leu Glu Glu Ser Ile Ala Asn 115 120 125

Leu Asn Arg Ser Thr Ser Val Pro Glu Asn Pro Lys Ser Ser Ala Ser 130 135 140

Thr Ala Val Ser Ala Ala Pro Thr Glu Lys Glu Phe Pro Lys Thr His 145 150 155 160

Ser Asp Val Ser Ser Glu Gln Gln His Leu Lys Gly Gln Thr Gly Thr 165 170 175

Asn Gly Gly Asn Val Lys Leu Tyr Thr Thr Asp Gln Ser Thr Phe Asp 180 185 190 Ile Leu Gln Asp Leu Glu Phe Ser Ser Gly Ser Pro Gly Lys Glu Thr 195 200 205 Asn Glu Ser Pro Trp Arg Ser Asp Leu Leu Ile Asp Glu Asn Cys Leu 210 215 220 Leu Ser Pro Leu Ala Gly Glu Asp Asp Ser Phe Leu Leu Glu Gly Asn 235 240 Ser Asn Glu Asp Cys Lys Pro Leu Ile Leu Pro Asp Thr Lys Pro Lys 245 250 255 Ile Lys Asp Asn Gly Asp Leu Val Leu Ser Ser Pro Ser Asn Val Thr 260 265 270 Leu Pro Gln Val Lys Thr Glu Lys Glu Asp Phe Ile Glu Leu Cys Thr 275 280 285 Pro Gly Val Ile Lys Gln Glu Lys Leu Gly Thr Val Tyr Cys Gln Ala 290 295 300 Ser Phe Pro Gly Ala Asn Ile Ile Gly Asn Lys Met Ser Ala Ile Ser 305 310 315 320 Val His Gly Val Ser Thr Ser Gly Gly Gln Met Tyr His Tyr Asp Met 325 330 335 Asn Thr Ala Ser Leu Ser Gln Gln Gln Asp Gln Lys Pro Ile Phe Asn 340 345 350 Val Ile Pro Pro Ile Pro Val Gly Ser Glu Asn Trp Asn Arg Cys Gln 355 360 365 Gly Ser Gly Asp Asp Asn Leu Thr Ser Leu Gly Thr Leu Asn Phe Pro 370 380 Gly Arg Thr Val Phe Ser Asn Gly Tyr Ser Ser Pro Ser Met Arg Pro 385 390 395 400 Asp Val Ser Ser Pro Pro Ser Ser Ser Ser Thr Ala Thr Thr Gly Pro 405 410 415 Pro Pro Lys Leu Cys Leu Val Cys Ser Asp Glu Ala Ser Gly Cys His 420 430 Tyr Gly Val Leu Thr Cys Gly Ser Cys Lys Val Phe Phe Lys Arg Ala

Val Glu Gly Gln His Asn Tyr Leu Cys Ala Gly Arg Asn Asp Cys Ile 450 455 460 Ile Asp Lys Ile Arg Arg Lys Asn Cys Pro Ala Cys Arg Tyr Arg Lys
465 470 475 480 Cys Leu Gln Ala Gly Met Asn Leu Glu Ala Arg Lys Thr Lys Lys 485 490 495 Ile Lys Gly Ile Gln Gln Ala Thr Thr Gly Val Ser Gln Glu Thr Ser Glu Asn Pro Gly Asn Lys Thr Ile Val Pro Ala Thr Leu Pro Gln Leu 515 520 525 Thr Pro Thr Leu Val Ser Leu Leu Glu Val Ile Glu Pro Glu Val Leu 530 540 Tyr Ala Gly Tyr Asp Ser Ser Val Pro Asp Ser Thr Trp Arg Ile Met Thr Thr Leu Asn Met Leu Gly Gly Arg Gln Val Ile Ala Ala Val Lys Trp Ala Lys Ala Ile Pro Gly Phe Arg Asn Leu His Leu Asp Asp Gln
580 585 590 Met Thr Leu Leu Gln Tyr Ser Trp Met Phe Leu Met Ala Phe Ala Leu Gly Trp Arg Ser Tyr Arg Gln Ser Ser Ala Asn Leu Leu Cys Phe Ala Pro Asp Leu Ile Ile Asm Glu Gln Arg Met Thr Leu Pro Cys Met Tyr Asp Gln Cys Lys His Met Leu Tyr Val Ser Ser Glu Leu His Arg Leu 650 655 Gln Val Ser Tyr Glu Glu Tyr Leu Cys Met Lys Thr Leu Leu Leu Leu 660 665 670 Ser Ser Val Pro Lys Asp Gly Leu Lys Ser Gln Glu Leu Phe Asp Glu 680 Ile Arg Met Thr Tyr Ile Lys Glu Leu Gly Lys Ala Ile Val Lys Arg
690 695 700 Glu Gly Asn Ser Ser Gln Asn Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser Met His Glu Val Val Glu Asn Leu Leu Asn Tyr Cys 725 730 735

Phe Gln Thr Phe Leu Asp Lys Thr Met Ser Ile Glu Phe Pro Glu Met 740 745 750

Leu Ala Glu Ile Ile Thr Asn Gln Ile Pro Lys Tyr Ser Asn Gly Asn 755 760 765

Ile Lys Lys Leu Leu Phe His Gln Lys 770 775

<210> 14

705

<211> 933

<212> PRT

<213> Homo sapiens

<400> 14

Met Thr Glu Leu Lys Ala Lys Gly Pro Arg Ala Pro His Val Ala Gly 1 5 10 15

Gly Pro Pro Ser Pro Glu Val Gly Ser Pro Leu Leu Cys Arg Pro Ala 20 25 30

Ala Gly Pro Phe Pro Gly Ser Gln Thr Ser Asp Thr Leu Pro Glu Val 35 40 45

Ser Ala Ile Pro Ile Ser Leu Asp Gly Leu Leu Phe Pro Arg Pro Cys 50 60

Gln Gly Gln Asp Pro Ser Asp Glu Lys Thr Gln Asp Gln Gln Ser Leu 70 75 80

Ser Asp Val Glu Gly Ala Tyr Ser Arg Ala Glu Ala Thr Arg Gly Ala 85 90 95

Gly Gly Ser Ser Ser Pro Pro Glu Lys Asp Ser Gly Leu Leu Asp 100 105 110

Ser Val Leu Asp Thr Leu Leu Ala Pro Ser Gly Pro Gly Gln Ser Gln 115 120 125

Pro Ser Pro Pro Ala Cys Glu Val Thr Ser Ser Trp Cys Leu Phe Gly 130 140

Pro Glu Leu Pro Glu Asp Pro Pro Ala Ala Pro Ala Thr Gln Arg Val 145 150 155 160

Leu Ser Pro Leu Met Ser Arg Ser Gly Cys Lys Val Gly Asp Ser Ser 165 170 175 Gly Thr Ala Ala Ala His Lys Val Leu Pro Arg Gly Leu Ser Pro Ala Arg Gln Leu Leu Pro Ala Ser Glu Ser Pro His Trp Ser Gly Ala 195 200 205 Pro Val Lys Pro Ser Pro Gln Ala Ala Ala Val Glu Val Glu Glu Glu Ser Ser Glu Ser Glu Glu Ser Ala Gly Pro Leu Leu Lys Gly Lys 230 235 240 Pro Pro Gly Ala Ala Ala Gly Gly Val Ala Leu Val Pro Lys Glu Asp 260 265 270 Ser Arg Phe Ser Ala Pro Arg Val Ala Leu Val Glu Gln Asp Ala Pro 275 280 285 Met Ala Pro Gly Arg Ser Pro Leu Ala Thr Thr Val Met Asp Phe Ile His Val Pro Ile Leu Pro Leu Asn His Ala Leu Leu Ala Ala Arg Thr 305 310 315 320 Arg Gln Leu Leu Glu Asp Glu Ser Tyr Asp Gly Gly Ala Gly Ala Ala 325 330 335 Ser Ala Phe Ala Pro Pro Arg Thr Ser Pro Cys Ala Ser Ser Thr Pro 340 345 350 Val Ala Val Gly Asp Phe Pro Asp Cys Ala Tyr Pro Pro Asp Ala Glu 355 360 365 Pro Lys Asp Asp Ala Tyr Pro Leu Tyr Ser Asp Phe Gln Pro Pro Ala Leu Lys Ile Lys Glu Glu Glu Glu Gly Ala Glu Ala Ser Ala Arg Ser 385 390 305 Pro Arg Ser Tyr Leu Val Ala Gly Ala Asn Pro Ala Ala Phe Pro Asp Phe Pro Leu Gly Pro Pro Pro Pro Leu Pro Pro Arg Ala Thr Pro Ser 420 425 430 Arg Pro Gly Glu Ala Ala Val Thr Ala Ala Pro Ala Ser Ala Ser Val 435 440 445 Ser Ala Ser Ser Ser Gly Ser Thr Leu Glu Cys Ile Leu Tyr Lys 450 460 Ala Glu Gly Ala Pro Pro Gln Gln Gly Pro Phe Ala Pro Pro Pro Cys Lys Ala Pro Gly Ala Ser Gly Cys Leu Leu Pro Arg Asp Gly Leu Pro Ser Thr Ser Ala Ser Ala Ala Ala Ala Gly Ala Ala Pro Ala Leu Tyr 500 505 510 Pro Ala Leu Gly Leu Asn Gly Leu Pro Gln Leu Gly Tyr Gln Ala Ala 515 520 525 Val Leu Lys Glu Gly Leu Pro Gln Val Tyr Pro Pro Tyr Leu Asn Tyr Leu Arg Pro Asp Ser Glu Ala Ser Gln Ser Pro Gln Tyr Ser Phe Glu Ser Leu Pro Gln Lys Ile Cys Leu Ile Cys Gly Asp Glu Ala Ser Gly 565 570 575 Cys His Tyr Gly Val Leu Thr Cys Gly Ser Cys Lys Val Phe Phe Lys 580 585 590 Arg Ala Met Glu Gly Gln His Asn Tyr Leu Cys Ala Gly Arg Asn Asp 595 600 605 Cys Ile Val Asp Lys Ile Arg Arg Lys Asn Cys Pro Ala Cys Arg Leu 610 620 Arg Lys Cys Cys Gln Ala Gly Met Val Leu Gly Gly Arg Lys Phe Lys 625 635 640 Lys Phe Asn Lys Val Arg Val Val Arg Ala Leu Asp Ala Val Ala Leu Pro Gln Pro Leu Gly Val Pro Asn Glu Ser Gln Ala Leu Ser Gln Arg Phe Thr Phe Ser Pro Gly Gln Asp Ile Gln Leu Ile Pro Pro Leu Ile

Asn Leu Leu Met Ser Ile Glu Pro Asp Val Ile Tyr Ala Gly His Asp 690 695 700 Asn Thr Lys Pro Asp Thr Ser Ser Ser Leu Leu Thr Ser Leu Asn Gln 705 710 715 720 Leu Gly Glu Arg Gln Leu Leu Ser Val Val Lys Trp Ser Lys Ser Leu Pro Gly Phe Arg Asn Leu His Ile Asp Asp Gln Ile Thr Leu Ile Gln 740 745 750 Tyr Ser Trp Met Ser Leu Met Val Phe Gly Leu Gly Trp Arg Ser Tyr 755 760 765 Lys His Val Ser Gly Gln Met Leu Tyr Phe Ala Pro Asp Leu Ile Leu 770 775 780 Asn Glu Gln Arg Met Lys Glu Ser Ser Phe Tyr Ser Leu Cys Leu Thr 785 790 795 800 Met Trp Gln Ile Pro Gln Glu Phe Val Lys Leu Gln Val Ser Gln Glu Glu Phe Leu Cys Met Lys Val Leu Leu Leu Leu Asn Thr Ile Pro Leu 820 825 830 Glu Gly Leu Arg Ser Gln Thr Gln Phe Glu Glu Met Arg Ser Ser Tyr Ile Arg Glu Leu Ile Lys Ala Ile Gly Leu Arg Gln Lys Gly Val Val 850 855 860 Ser Ser Ser Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Asn Leu 865 870 875 His Asp Leu Val Lys Gln Leu His Leu Tyr Cys Leu Asn Thr Phe Ile 885 890 895 Gln Ser Arg Ala Leu Ser Val Glu Phe Pro Glu Met Met Ser Glu Val 900 905 910 Ile Ala Ala Gln Leu Pro Lys Ile Leu Ala Gly Met Val Lys Pro Leu 915 920 925

Leu Phe His Lys Lys

930

<210> 15

<211> 984

<212> PRT

<213> Homo sapiens

<400> 15

Met Glu Thr Lys Gly Tyr His Ser Leu Pro Glu Gly Leu Asp Met Glu 10 15

Arg Arg Trp Gly Gln Val Ser Gln Ala Val Glu Arg Ser Ser Leu Gly
20 25 30

Pro Thr Glu Arg Thr Asp Glu Asn Asn Tyr Met Glu Ile Val Asn Val · 35 40 45

Ser Cys Val Ser Gly Ala Ile Pro Asn Asn Ser Thr Gln Gly Ser Ser 50 60

Lys Glu Lys Gln Glu Leu Leu Pro Cys Leu Gln Gln Asp Asn Asn Arg 65 70 75 80

Pro Gly Ile Leu Thr Ser Asp Ile Lys Thr Glu Leu Glu Ser Lys Glu 85 90 95

Leu Ser Ala Thr Val Ala Glu Ser Met Gly Leu Tyr Met Asp Ser Val 100 105 110

Arg Asp Ala Asp Tyr Ser Tyr Glu Gln Gln Asn Gln Gln Gly Ser Met 115 120 125

Ser Pro Ala Lys Ile Tyr Gln Asn Val Glu Gln Leu Val Lys Phe Tyr 130 . 135 140

Lys Gly Asn Gly His Arg Pro Ser Thr Leu Ser Cys Val Asn Thr Pro 145 150 155 160

Leu Arg Ser Phe Met Ser Asp Ser Gly Ser Ser Val Asn Gly Gly Val 165 170 175

Met Arg Ala Ile Val Lys Ser Pro Ile Met Cys His Glu Lys Ser Pro 180 185 190

Ser Val Cys Ser Pro Leu Asn Met Thr Ser Ser Val Cys Ser Pro Ala 195 200 205

Gly Ile Asn Ser Val Ser Ser Thr Thr Ala Ser Phe Gly Ser Phe Pro 210 220

Val His Ser Pro Ile Thr Gln Gly Thr Pro Leu Thr Cys Ser Pro Asn Ala Glu Asn Arg Gly Ser Arg Ser His Ser Pro Ala His Ala Ser Asn 245 250 255 Val Gly Ser Pro Leu Ser Ser Pro Leu Ser Ser Met Lys Ser Ser Ile Ser Ser Pro Pro Ser His Cys Ser Val Lys Ser Pro Val Ser Ser Pro 275 280 285 Asn Asn Val Thr Leu Arg Ser Ser Val Ser Ser Pro Ala Asn Ile Asn Asn Ser Arg Cys Ser Val Ser Ser Pro Ser Asn Thr Asn Asn Arg Ser Thr Leu Ser Ser Pro Ala Ala Ser Thr Val Gly Ser Ile Cys Ser Pro Val Asn Asn Ala Phe Ser Tyr Thr Ala Ser Gly Thr Ser Ala Gly Ser Ser Thr Leu Arg Asp Val Val Pro Ser Pro Asp Thr Gln Glu Lys Gly Ala Gln Glu Val Pro Phe Pro Lys Thr Glu Glu Val Glu Ser Ala Ile Ser Asn Gly Val Thr Gly Gln Leu Asn Ile Val Gln Tyr Ile Lys Pro 385 390 395 400 Glu Pro Asp Gly Ala Phe Ser Ser Cys Leu Gly Gly Asn Ser Lys 405 410 415 Ile Asn Ser Asp Ser Ser Phe Ser Val Pro Ile Lys Gln Glu Ser Thr 420 425 430 Lys His Ser Cys Ser Gly Thr Ser Phe Lys Gly Asn Pro Thr Val Asn Pro Phe Pro Phe Met Asp Gly Ser Tyr Phe Ser Phe Met Asp Asp Lys 450 455 460 Asp Tyr Tyr Ser Leu Ser Gly Ile Leu Gly Pro Pro Val Pro Gly Phe Asp Gly Asn Cys Glu Gly Ser Gly Phe Pro Val Gly Ile Lys Gln Glu 490

Pro Asp Asp Gly Ser Tyr Tyr Pro Glu Ala Ser Ile Pro Ser Ser Ala 500 505 510 Ile Val Gly Val Asn Ser Gly Gly Gln Ser Phe His Tyr Arg Ile Gly 515 520 525 Ala Gln Gly Thr Ile Ser Leu Ser Arg Ser Ala Arg Asp Gln Ser Phe 530 540 Gln His Leu Ser Ser Phe Pro Pro Val Asn Thr Leu Val Glu Ser Trp 545 550 555 560 Lys Ser His Gly Asp Leu Ser Ser Arg Arg Ser Asp Gly Tyr Pro Val 565 570 575 Leu Glu Tyr Ile Pro Glu Asn Val Ser Ser Ser Thr Leu Arg Ser Val 580 585 590 Ser Thr Gly Ser Ser Arg Pro Ser Lys Ile Cys Leu Val Cys Gly Asp 595 600 605 Glu Ala Ser Gly Cys His Tyr Gly Val Val Thr Cys Gly Ser Cys Lys 610 615 620 Val Phe Phe Lys Arg Ala Val Glu Gly Gln His Asn Tyr Leu Cys Ala 625 630 635 640 Gly Arg Asn Asp Cys Ile Ile Asp Lys Ile Arg Arg Lys Asn Cys Pro 645 650 655 Ala Cys Arg Leu Gln Lys Cys Leu Gln Ala Gly Met Asn Leu Gly Ala 660 665 670 Arg Lys Ser Lys Lys Leu Gly Lys Leu Lys Gly Ile His Glu Glu Gln 675 680 685 Pro Gln Gln Gln Pro Pro Pro Pro Pro Pro Pro Gln Ser Pro 690 695 700 Glu Glu Gly Thr Thr Tyr Ile Ala Pro Ala Lys Glu Pro Ser Val Asn 705 710 715 720 Thr Ala Leu Val Pro Gln Leu Ser Thr Ile Ser Arg Ala Leu Thr Pro
725 730 735

Ser Pro Val Met Val Leu Glu Asn Ile Glu Pro Glu Ile Val Tyr Ala 740 745 750 Gly Tyr Asp Ser Ser Lys Pro Asp Thr Ala Glu Asn Leu Leu Ser Thr 755 760 765 Leu Asn Arg Leu Ala Gly Lys Gln Met Ile Gln Val Val Lys Trp Ala 770 780 Lys Val Leu Pro Gly Phe Lys Asn Leu Pro Leu Glu Asp Gln Ile Thr 785 790 795 800 Leu Ile Gln Tyr Ser Trp Met Cys Leu Ser Ser Phe Ala Leu Ser Trp 810 Arg Ser Tyr Lys His Thr Asn Ser Gln Phe Leu Tyr Phe Ala Pro Asp 825 Leu Val Phe Asn Glu Glu Lys Met His Gln Ser Ala Met Tyr Glu Leu Cys Gln Gly Met His Gln Ile Ser Leu Gln Phe Val Arg Leu Gln Leu Thr Phe Glu Glu Tyr Thr Ile Met Lys Val Leu Leu Leu Ser Thr lle Pro Lys Asp Gly Leu Lys Ser Gln Ala Ala Phe Glu Glu Met Arg 885 890 895 Thr Asn Tyr Ile Lys Glu Leu Arg Lys Met Val Thr Lys Cys Pro Asn Asn Ser Gly Gln Ser Trp Gln Arg Phe Tyr Gln Leu Thr Lys Leu Leu 915 920 925 Asp Ser Met His Asp Leu Val Ser Asp Leu Leu Glu Phe Cys Phe Tyr 930

Val Glu Ile Ile Ser Asp Gln Leu Pro Lys Val Glu Ser Gly Asn Ala 965 970 975

Thr Phe Arg Glu Ser His Ala Leu Lys Val Glu Phe Pro Ala Met Leu

Lys Pro Leu Tyr Phe His Arg Lys 980

<210> 16 <211> 452 <212> PRT <213> Homo sapiens

<400> 16

Gly Gly Gly Gly Glu Ala Gly Ala Val Ala Pro Tyr Gly Tyr Thr 1 5 10 15

Arg Pro Pro Gln Gly Leu Ala Gly Gln Glu Ser Asp Phe Thr Ala Pro
20 25 30

Asp Val Trp Tyr Pro Gly Gly Met Val Ser Arg Val Pro Tyr Pro Ser 35 40 45

Pro Thr Cys Val Lys Ser Glu Met Gly Pro Trp Met Asp Ser Tyr Ser 50 60

Gly Pro Tyr Gly Asp Met Arg Leu Glu Thr Ala Arg Asp His Val Leu 65 70 75 80

Pro Ile Asp Tyr Tyr Phe Pro Pro Gln Lys Thr Cys Leu Ile Cys Gly 85 90 95

Asp Lys Ala Ser Gly Cys His Tyr Gly Ala Leu Thr Cys Gly Ser Cys 100 105 110

Lys Val Phe Phe Lys Arg Ala Ala Glu Gly Lys Gln Lys Tyr Leu Cys 115 120 125

Ala Ser Arg Asn Asp Cys Thr Ile Asp Lys Phe Arg Arg Lys Asn Cys 130 135 140

Pro Ser Cys Arg Leu Arg Lys Cys Tyr Glu Ala Gly Met Thr Leu Gly 145 150 155 160

Ala Arg Lys Leu Lys Lys Leu Gly Asn Leu Lys Leu Gln Glu Gly 165 170 175

Glu Ala Ser Ser Thr Thr Ser Pro Thr Glu Glu Thr Thr Gln Lys Leu 180 185 190

Thr Val Ser His Ile Glu Gly Tyr Glu Cys Gln Pro Ile Phe Leu Asn 195 200 205

Val Leu Glu Ala Ile Glu Pro Gly Val Val Cys Ala Gly His Asp Asn 210 215 220

Asn Gln Pro Asp Ser Phe Ala Ala Leu Leu Ser Ser Leu Asn Glu Leu 225 230 235 240

Gly Glu Arg Gln Leu Val His Val Val Lys Trp Ala Lys Ala Leu Pro

Gly Phe Arg Asn Leu His Val Asp Asp Gln Met Ala Val Ile Gln Tyr 260 265 270

Ser Trp Met Gly Leu Met Val Phe Ala Met Gly Trp Arg Ser Phe Thr 275 280 285

Asn Val Asn Ser Arg Met Leu Tyr Phe Ala Pro Asp Leu Val Phe Asn 290 295 300

Glu Tyr Arg Met His Lys Ser Arg Met Tyr Ser Gln Cys Val Arg Met 305 310 315 320

Arg His Leu Ser Gln Glu Phe Gly Trp Leu Gln Ile Thr Pro Gln Glu 325 330 335

Phe Leu Cys Met Lys Ala Leu Leu Leu Phe Ser Ile Ile Pro Val Asp 340 345 350

Gly Leu Lys Asn Gln Lys Phe Phe Asp Glu Leu Arg Met Asn Tyr Ile 355 360 365

Lys Glu Leu Asp Arg Ile Ile Ala Cys Lys Arg Lys Asn Pro Thr Ser 370 380

Cys Ser Arg Arg Phe Tyr Gln Leu Thr Lys Leu Leu Asp Ser Val Gln 385 390 395

Pro Ile Ala Arg Glu Leu His Gln Phe Thr Phe Asp Leu Leu Ile Lys 405 410 415

Ser His Met Val Ser Val Asp Phe Pro Glu Met Met Ala Glu Ile Ile 420 425 430

Ser Val Gln Val Pro Lys Ile Leu Ser Gly Lys Val Lys Pro Ile Tyr 435 440 445

Phe His Thr Gln 450